UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/332,866	06/15/1999	BEATRICE LEVEUGLE	A52026US	3446

7590 02/27/2002

NANCY CHIU, PH.D.
HALE AND DORR LLP
60 STATE STREET
BOSTON, MA 02109

EXAMINER
DAVIS, MINH TAM B

ART UNIT	PAPER NUMBER
1642	# 19

DATE MAILED: 02/27/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/332,866	LEVEUGLE ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14,15,17,20,21 and 28-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14,15,17,20,21 and 28-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *14,16* . (8 sheets)
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The request filed on 11/20/01 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No:09/332866 is acceptable and a CPA has been established. An action on the CPA follows.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant adds new claims 28-34, which are related to claims 14, 15, 17, 20 and 21 and are not new matters.

Accordingly, claims 14, 15, 17, 20-21 and 28-34 are being examined.

The following are the remaining rejections.

DEPOSIT REQUIREMENT

Rejection remains because Applicant has not submitted an affidavit or declaration stating not only that all restrictions upon public access to the desposits will be irrevocably removed upon the grant of a patent on this application but also that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, ENABLEMENT

Rejection under 35 USC 112, first paragraph of claims 14, 15, 17, 20-21 pertaining to lack of enablement for a method for inducing an immune response to prostate specific antigen remains for reasons already of record in paper No.15. New claims 28-34 are rejected for the same reasons already of record in paper No.15.

New claims 28-34 are drawn to a method for inducing a host to produce an antibody specific for prostate specific antigen, comprising administrating to the host a binding agent that specifically binds to an epitope of circulating prostate specific antigen, wherein the epitope is specifically bound by a monoclonal antibody produced by the hybridoma HB-12526.

Applicant asserts that the host in claims 28-34 need not be suffering from prostate cancer, nor have any circulating prostate specific antigen.

Applicant further asserts that in Examples 7, and 11, the tumor burden of mice is considerably lower when the mice are immunized with anti-PSA antibody or antibody AR47.47, as compared to animals treated with control antibody or PBS. In addition Applicant asserts that page 36, lines 11-14 of the specification discloses that "the positive signal obtained for Ab3 in the control groups (PBS and contral mAb) is not surprising, since the release of human PSA by the growing tumor in vivo will induce an anti-PSA immune response. Further, in Example 12, the animal is already inoculated with tumor cells, the therapeutic effect of AR47.47 upon tumor burden would have been disguised, since the animal itself would have been making its own anti-PSA antibodies, which would then compete with AR47.47 in binding to circulating PSA. This is why no therapeutic effect was observed in Example 12. Applicant concludes that thus one of

skill in the art would know, upon reading in the Application that administration of AR47.47 induces anti-PSA antibodies in a prostate-cancer free host, that administration of AR47.47 to a prostate cancer patient would likewise induce anti-PSA antibodies in the prostate cancer patient.

Applicant's arguments set forth in paper No.18 have been considered but are not deemed to be persuasive for the following reasons:

It is noted a "host" in claims 28-34 encompasses a host having prostate cancer, besides a host free of prostate cancer. It is further noted that in Examples 7 and 11, although the tumor burden in mice treated with the claimed antibodies is lower than the controls, the mice are cancer-free while being treated with the claimed antibodies before injection of a tumor cell line. In addition, it is noted that in Example 12, the treated mice have had tumor, and that there is no therapeutic effect of the claimed antibody AR47.47.

It is unpredictable that the claimed method could produce an immune response or antibody specific for prostate specific antigen in a host or a patient having prostate cancer, in view of Example 12, wherein the treated mice have had tumor, and there is no therapeutic effect of the claimed antibody AR47.47. The problem with T cell anergy in the presence of a tumor burden, and self-tolerance is well known in the art. Sherman, LA et al, 1998, Critical reviews in Immunol, 18(1-2): 47-54 teach that self-tolerance may eliminate T cells that are capable of recognizing those epitopes with high avidity. Thus, since PSA is a self-antigen, it is unpredictable that in human patients with prostate cancer, the claimed antibodies would produce adequate number of CTLs with

high affinity which are optimal for interacting with the antigen. Further, it is also well known in the art that in animals or humans bearing tumor burden, the cytotoxic or proliferative responses of tumor-specific T cells are blocked, i.e. T-cells anergy, due to excess presence of the antigen (Smith, MD, 1994, Clinical Immunol, 41: 841-850, especially p. 848). Thus, since there is immune suppression in patients with tumor burden, it is unpredictable that proliferative T cells that are needed for B cells activation and producing antibodies specific for the claimed PSA sequence of SEQ ID NO:1 would not be anergic in human patients with tumor burden.

Thus one could not deduce from the fact that the claimed antibody AR47.47 induces anit-idiotypic antibodies against PSA in prostate cancer-free host that the claimed antibody AR47.47 would also induce anti-PSA antibodies in prostate cancer host.

Moreover, concerning treating a prostate cancer-free host to prevent prostate cancer, Applicant has not shown how to identify or predict which prostate cancer-free host would develop prostate cancer, nor exactly when to administer the claimed antibody to a prostate cancer-free host, especially in view of the fact that prostate cancer is a very slow progressing disease, and different from the model in mice, wherein in mice the growth rate of the tumor is much faster, as disclosed in the specification on page 39.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE

Rejection under 35 USC 112, first paragraph of claims 14, 15, 17, 20-21 pertaining to lack of enablement for a method for inducing an immune response to prostate specific antigen, comprising administering "any binding agent" that specifically binds to an epitope of circulating prostate specific antigen, wherein the epitope is specifically bound by a monoclonal antibody produced by the hybridoma HB-12526, remains for reasons already of record in paper No.15. New claims 28-34 are rejected for the same reasons already of record in paper No.15.

New claims 28-34 are drawn to a method for inducing a host to produce an antibody specific for prostate specific antigen, comprising administrating to the host a binding agent that specifically binds to an epitope of circulating prostate specific antigen, wherein the epitope is specifically bound by a monoclonal antibody produced by the hybridoma HB-12526.

Applicant asserts that one would understand that any binding agent, as described in the specification on page 10, line 16 through page 11, line 12, that specifically binds to the same epitope to which the monoclonal antibodie AR47.47 specifically binds would accomplish the same result. Applicant further asserts that to limit Applicant to their exemplary binding agent would be unjust, considering the scope of what is taught in the specification and what was known in the art at the time the invention was make.

Applicant's arguments set forth in paper No.18 have been considered but are not deemed to be persuasive for the following reasons:

The specification on page 10, line 16 through page 11, line 12 discloses that exemplary binding agents include, "but are not limited to" monoclonal antibodies, chimeric antibodies, fragments thereof, single chain antibodies, tumor binding peptides, mimics of any of the above, and variants the antibodies. The specification further discloses that production of an immune response includes production of anti-idiotypic antibodies and anti-anti-idiotypic antibodies which are anti-PSA.

The scope of the claims encompasses administration of any compound that binds to the epitope to which the monoclonal antibody AR47.47 specifically binds, for example any binding label or any peptide or non-peptide agonist or antagonist of the claimed antibody AR47.47, the structure of which is completely different than the structure of an antibody which specifically binds to SEQ ID NO:1, or of SEQ ID NO:1, wherein said compound would produce an immune response to prostate specific antigen , or anti-idiotypic antibodies and anti-anti-idiotypic antibodies which are specifically anti-PSA.

It is well known in the art that anti-idiotypic antibodies or Ab2 are produced from the first antibody, and recognize the sequence in the hypervariable regions of the target antibody, which are unique to that antibody and determine its antigen specificity (Stites et al, eds, 1997, Medical Immunol, Appleton& Lange, Connecticut, p.103, second column, idiotypes section).

Thus one of skill in the art would not have expected that any binding agent would produce an immune response to prostate specific antigen or an antibody specific for

prostate specific antigen, because the structure of said binding agent could be totally unrelated to prostate specific antigen, or the claimed antibody AR47.47.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE, NEW REJECTION

If Applicant could overcome the above 112, first paragraph rejection, claims 28-34 are still rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for inducing a host to produce an anti-idiotypic antibody (Ab2) specific for prostate specific antigen, does not reasonably provide enablement for a method for inducing a host to produce "an antibody"specific for prostate specific antigen. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

New claims 28-34 are drawn to a method for inducing a host to produce an antibody specific for prostate specific antigen, comprising administrating to the host a binding agent that specifically binds to an epitope of circulating prostate specific antigen, wherein the epitope is specifically bound by a monoclonal antibody produced by the hybridoma HB-12526.

Claims 28-34 encompass a method for inducing a host to produce any antibody specific for prostate specific antigen, i.e. anti-anti-idiotypic antibodies (Ab3), comprising administrating to the host a binding agent that specifically binds to an epitope of circulating prostate specific antigen, wherein the epitope is specifically bound by a monoclonal antibody produced by the hybridoma HB-12526.

It is unpredictable that administration of the claimed antibody AR47.47 would produce an anti-anti-idiotypic antibody which recognizes the epitope consisting of SEQ ID NO:1, i.e. the epitope which is specifically bound by a monoclonal antibody produced by the hybridoma HB-12526, or antibody AR47.47. The specification discloses that the presence of Ab3 could only be found when a tested plate is coated with PSA, i.e. detecting the binding of Ab3 and PSA, whereas an assay using the claimed PSA peptide of SEQ ID NO:1 to coat the plate has not been standardized at the time of filing the instant application, because in many cases the positive control performed with the antibody AR47.47 shows negative signal (p.31). Thus it is possible that the Ab3 detected by Applicant is an antibody that binds to an epitope different from SEQ ID NO:1.

In view of the above, it would have been undue experimentation for one of skill in the art at the time the invention was made to practice the claimed invention.

REJECTION UNDER 35 USC 102

Rejection under 35 USC 102 of claims 14, 15, 17, pertaining to anticipation by Giri et al, remains for reasons already of record in paper No.15. New claims 28-31, 34 are rejected for the same reasons already of record in paper No.15.

New claims 28-31, 34 are drawn to or a method for inducing a host to produce an antibody specific for prostate specific antigen, comprising administrating to the host a binding agent that specifically binds to an epitope of circulating prostate specific

antigen, wherein the epitope is specifically bound by a monoclonal antibody produced by the hybridoma HB-12526.

Applicant argues that Giri et al do not teach a binding agent that specifically binds to an epitope of circulating prostate specific antigen, wherein the epitope is specifically bound by a monoclonal antibody produced by the hybridoma HB-12526.

Applicant's arguments set forth in paper No.18 have been considered but are not deemed to be persuasive for the following reasons:

Giri et al teach administration of polyclonal antibodies specific for PSA. Thus the method taught by Giri et al is the same as the claimed method, because the polyclonal antibodies taught by Giri et al would inherently have a subpopulation of antibodies that specifically bind to an epitope of circulating prostate specific antigen, wherein the epitope is specifically bound by a monoclonal antibody produced by the hybridoma HB-12526, and because the claimed are not drawn to administration of "monoclonal antibodies" specific for an epitope of circulating prostate specific antigen, wherein the epitope is specifically bound by a monoclonal antibody produced by the hybridoma HB-12526.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 703-305-2008. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANTHONY CAPUTA can be reached on 703-308-3995. The fax phone

numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.

MINH TAM DAVIS

February 19, 2002

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600